AMENDMENTS TO THE SPECIFICATION

Please replace the title with the following:

~~HUMAN AND~~POLYNUCLEOTIDE ENCODING A MOUSE CHOLINE TRANSPORTER cDNA

Please replace the paragraph bridging pages 2-3 with:

Okuda *et al.* (2000) have identified and characterized a high-affinity choline transporter in the rat. However, using human gene products in drug development offers significant advantages over those of other species, which may not exhibit the same pharmacological profiles as human genes. Reagents developed to interfere or modulate the rat transporter may not be as clinically relevant as reagents developed using a human system. Also, since no cell lines exist which express the human choline transporter, lack of crossreactivity must be validated using less ideal tissue, for example, postmortem brain tissue. Okuda *et al.* (2000) provides no sequence relationship between rat and human choline transporters. Also, the Okuda's proposed topology for rat choline transporters is distinct from the topology as described herein. Okuda *et al.* proposes 12 transmembrane domains for rat and *C. elegans* choline transporters. However, human (Apparsundaram *et al.* 2000) and mouse (Apparsundaram *et al.*, ~~2001 in press~~*Biochem. Soc. Trans.* 29:711-6, 2001) choline transporters were not described, and these transporters have a distinct protein topology (13 transmembrane domains) based on the sequence relationship of cDNAs to related Na+/glucose family of transporters.

Please replace the paragraph bridging page 8-9 with:

FIG. 2 - Alignment of amino acid sequence of high-affinity choline transporters. Alignment of mCHT with species orthologs was performed using version 1.6.3 of Lasergene software. Abbreviations are as follows: mCHT, murine (SEQ ID NO:4); hCHT, human (SEQ ID NO:2); rCHT, rat (SEQ ID NO:6; CHO-1, *Caenorhabtiditis elegans* (SEQ ID NO:8); ChCoT, *Limulus polyphemus*. Residues matching mCHT sequences are blackened. Residues spanning

putative TMDs inferred from hydropathy analysis are represented by line drawn above the sequences.

Please replace the paragraph starting at page 9, line 9, with:

FIG. 4 - Predicted hCHT amino acid sequence (SEQ ID NO:2). Amino acid sequence of the derived from hCHT. The location of 13 TMDs are shown with solid lines above the corresponding amino acid residues. Asterisks indicate potential extracellular N-glycosylation sites.

Please replace the paragraph bridging pages 10-11 with:

FIGS. 11A - 11D - High-affinity choline uptake and hemicholinium-3 binding sites are evident following transient expression of mCHT in COS-7 cells. Resealed membrane vesicles obtained from mCHT transfected COS-7 cells exhibit saturable and high-affinity choline uptake. Insets are Eadie-Hofstee transformations of mCHT-mediated choline uptake in resealed membrane vesicles (FIG. 11A). Unlabeled HC-3, choline and ACh dose-dependently inhibit [^{3}H] choline uptake in resealed membrane vesicles of COS-7 cells (FIG. 11B). Unlabeled HC-3, choline and acetylcholine were co-incubated with labeled HC-3. (FIG. 11C) [^{3}H] HC-3 binding as a function of HC-3 concentration. (FIG. 11D) Inhibition of [^{3}H] HC-3 binding as a function o inhibitor concentration.

Please replace the paragraph starting at line 10 of page 11 with:

~~FIG. 14~~**FIGS. 14A-B** - ~~Image~~Images of ChT-ir fibers in the hippocampus. Choline transporter antibodies reveal cholinergic fibers in the mouse hippocampus.

Please replace the paragraph bridging pages 20-21 with:

Proteinaceous compositions may be made by any technique known to those of skill in the art, including the expression of proteins, polypeptides or peptides through standard molecular biological techniques, the isolation of proteinaceous compounds from natural sources, or the

chemical synthesis of proteinaceous materials. The nucleotide and protein, polypeptide and peptide sequences for various genes have been previously disclosed, and may be found at computerized databases known to those of ordinary skill in the art. One such database is the National Center for Biotechnology Information's Genbank and GenPept databases (http://www.ncbi.nlm.nih.gov/). The coding regions for these known genes may be amplified and/or expressed using the techniques disclosed herein or as would be know to those of ordinary skill in the art. Alternatively, various commercial preparations of proteins, polypeptides and peptides are known to those of skill in the art.

Please replace the paragraph at the bottom of 25 with:

The term "functionally equivalent codon" is used herein to refer to codons that encode the same amino acid, such as the six codons for arginine and serine, and also refers to codons that encode biologically equivalent amino acids. For optimization of expression of hCHT or mCHT in human cells, the codons are shown in Table 2 in preference of use from left to right. Thus, the most preferred codon for alanine is thus "GCC," and the least is "GCG" (see Table 2 below). Codon usage for various organisms and organelles can be found at the website http://www.kazusa.or.jp/codon/, incorporated herein by reference, allowing one of skill in the art to optimize codon usage for expression in various organisms using the disclosures herein. Thus, it is contemplated that codon usage may be optimized for other animals, as well as other organisms such as a prokaryote (*e.g.*, an eubacteria), an archaea, an eukaryote (*e.g.*, a protist, a plant, a fungus, an animal), a virus and the like, as well as organelles that contain nucleic acids, such as mitochondria or chloroplasts, based on the preferred codon usage as would be known to those of ordinary skill in the art.

Please replace the paragraph at the bottom of 46 with:

Additionally any promoter/enhancer combination (as per the Eukaryotic Promoter Data Base EPDB, http://www.epd.isb-sib.ch/) could also be used to drive expression. Use of a T3, T7 or SP6 cytoplasmic expression system is another possible embodiment. Eukaryotic cells can support cytoplasmic transcription from certain bacterial promoters if the appropriate bacterial

polymerase is provided, either as part of the delivery complex or as an additional genetic expression construct.

Please replace the paragraph bridging pages 136-137 with:

Immunocytochemistry reveal cholinergic neurons, terminals, fibers, synapses and other tissues associated with cholinergic function. Green fluorescent protein, or other visible markers can be used, suc a β-glacticidase (See, for example U.S. Patent ~~Application 09/888,233~~6,894,205). Images of ChTt-ir in striatum and basal ganglia (FIG. 12), septum (FIG. 13), hipocampus. (FIG. 14), medulla oblongata (FIG. 15), neuromuscular junction of the diaphragm (FIG. 16) and the neuromuscular junction of the bladder (FIG. 17) demonstrate the use of immunocytochemistry for determining cholinerigic associated tissues. These images reveal the choline transporter antibodies stainging of cholinergic neurons and terminals in the mouse striatum and basal forebrain (FIG. 12) cholinergic neurons and processes in the septal nucleus (FIG. 13), cholinergic fibers in the mouse hippocampus (FIG. 14), cholinergic motor neurons in the brainstem (FIG. 15), cholinergic synapses on muscle cell (FIG. 16) and parasympathetic neuronal terminals on smooth muscle in the bladder.